Superiority in quality of life improvement of biologics over conventional systemic drugs in a swiss real-life psoriasis registry

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Abstract: BACKGROUND: Randomized controlled trials have shown the efficacy of systemic treatments in moderate-to-severe psoriasis. Clinical outcomes in psoriasis patients under real-world conditions are less well understood. OBJECTIVE: This study compared Psoriasis Area and Severity Index (PASI) and Dermatological Life Quality Index (DLQI) improvement in all psoriasis patients registered in the Swiss Dermatology Network for Targeted Therapies. We asked whether outcomes differed between 4 treatment strategies, namely biologic monotherapy versus conventional systemic monotherapy, versus combined biologic and conventional systemic drugs, and versus therapy adaptation (switching from one type to another). METHODS: PASI and DLQI within 1 year after onset of systemic treatment, measured at 3, 6, and 12 months, were compared among the 4 groups using generalized linear mixed-effects models. RESULTS: Between March 2011 and December 2014, 334 patients were included; 151 received conventional systemic therapeutics, 145 biologics, 13 combined treatment, and 25 had a therapy adaptation. With regard to the absolute PASI, neither the biologic cohort nor the combined treatment cohort significantly differed from the conventional systemic therapeutics cohort. The odds of reaching PASI90 was significantly increased with combined therapy compared to conventional systemic therapeutics ($p = 0.043$) and decreased with a higher body mass index ($p = 0.041$). At visits 3 and 4, the PASI was generally lower than at visit 2 (visit 3 vs. visit 2, $p = 0.0019$; visit 4 vs. visit 2, $p < 0.001$). After 12 months, patients with biologic treatment had a significantly lower DLQI than those with conventional systemic therapeutics ($p = 0.001$). CONCLUSION: This study suggests that after 1 year of treatment, biologics are superior in improving the subjective disease burden compared to conventional systemic drugs.

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Superiority in Quality of Life Improvement of Biologics over Conventional Systemic Drugs in a Swiss Real-Life Psoriasis Registry

Pierre Jungo[a] Julia-Tatjana Maul[c] Vahid Djamei[c] Stefanie von Felten[b] Antonios G.A. Kolios[c, d] Justine Czernielewsk[e] Nikhil Yawalkar[f] Olivia Odermatt[g] Emmanuel Laffitte[i] Mark Anliker[g] Markus Streit[h] Matthias Augustin[j] Curdin Conrad[b] Jürg Hafner[c] Wolf-Henning Boehncke[i] Michel Gilliet[e] Peter Itin[a] Lars E. French[c] Alexander A. Navarini[c] Peter Häusermann[a]

[a]Department of Dermatology, and [b]Clinical Trial Unit, University Hospital Basel, Basel, Departments of [c]Dermatology and [d]Immunology, University Hospital Zurich, Zurich, [e]Department of Dermatology, Centre Hospitalier Universitaire Vaudois, Lausanne, [f]Department of Dermatology, University Hospital Bern, Bern, [g]Department of Dermatology, Hospital St. Gallen, St. Gallen, [h]Department of Dermatology, Hospital Aarau, Aarau, and [i]Department of Dermatology, Hôpitaux Universitaires de Genève, Geneva, Switzerland; [j]Competenzzentrum Versorgungsforschung in der Dermatologie, Hamburg, Germany

Keywords

Psoriasis · Dermatological Life Quality Index · Psoriasis Area and Severity Index · Real world · Registry data · Biologicals

Abstract

Background: Randomized controlled trials have shown the efficacy of systemic treatments in moderate-to-severe psoriasis. Clinical outcomes in psoriasis patients under real-world conditions are less well understood. ***Objective:*** This study compared Psoriasis Area and Severity Index (PASI) and Dermatological Life Quality Index (DLQI) improvement in all psoriasis patients registered in the Swiss Dermatology Network for Targeted Therapies. We asked whether outcomes differed between 4 treatment strategies, namely biologic monotherapy versus conventional systemic monotherapy, versus combined biologic and conventional systemic drugs, and versus therapy adaptation (switching from one type to another). ***Methods:*** PASI and DLQI within 1 year after onset of systemic treatment, measured at 3, 6, and 12 months, were compared among the 4 groups using generalized linear mixed-effects models. ***Results:*** Between March 2011 and December 2014, 334 patients were included; 151 received conventional systemic therapeutics, 145 biologics, 13 combined treatment, and 25 had a therapy adaptation. With regard to the absolute PASI, neither the biologic cohort nor the combined treatment cohort significantly differed from the conventional systemic therapeutics cohort. The odds of reaching PASI90 was significantly increased with combined therapy compared to conventional systemic therapeutics ($p = 0.043$) and decreased with a higher body mass index ($p = 0.041$). At visits 3 and 4, the PASI was generally lower than at visit 2 (visit 3 vs. visit 2, $p = 0.0019$; visit 4 vs. visit 2, $p < 0.001$). After 12 months, patients with biologic treatment

Pierre Jungo and Julia-Tatjana Maul share the first authorship. Alexander A. Navarini and Peter Häusermann share the last authorship.

Prof. Dr. Peter Häusermann
Department of Dermatology, University Hospital Basel
Petersgraben 4
CH–4031 Basel (Switzerland)
E-Mail peter.haeusermann@usb.ch

had a significantly lower DLQI than those with conventional systemic therapeutics (p = 0.001). ***Conclusion:*** This study suggests that after 1 year of treatment, biologics are superior in improving the subjective disease burden compared to conventional systemic drugs.

Introduction

Of about 8.2 million people living in Switzerland, up to 360,000 suffer from psoriasis [1, 2], and between 8,200 and 32,400 may have moderate-to-severe psoriasis. The latter condition has a profound impact on the quality of life of patients and their respective risk to develop or worsen diseases of civilization such as cardiovascular events [3, 4]. Although randomized controlled trials have shown efficacy of most systemic treatments [5–7], profound knowledge about long-term outcomes and optimal treatment strategies in specific patients under real-world conditions are lacking in Switzerland. The Swiss Dermatology Network for Targeted Therapies (SDNTT) registry was established in 2011 to study the efficacy and safety of approved systemic therapies and patient-reported measures in real-life settings over time [8]. In contrast to randomized clinical trials, patient registries have less stringent inclusion criteria and allow to follow heterogeneous patient populations with varying disease severity and medications for long periods of time [9, 10]. We were particularly interested to compare the development of the PASI (Psoriasis Area and Severity Index) and DLQI (Dermatological Life Quality Index) within the first year of onset of treatment in all Swiss psoriasis patients included in the SDNTT who were treated with biologics only, biologics and conventional systemic therapeutics (simultaneously) or therapy adaptation (switching from one type to the other) with those who were treated with conventional systemic therapeutics only. The SDNTT is a non-interventional observational registry based on an electronic case report form provided by the Centre of Excellence for Health Services Research in Dermatology (CVderm, Competenzzentrum Versorgungsforschung in der Dermatologie) at the University Medical Center Hamburg Eppendorf, Germany. The documentation is managed using a patient-based database as a registry.

Patients and Methods

For further details, see the supplementary materials (for all online suppl. material, see www.karger.com/doi/10.1159/000455042 [11–18] (Fig. 1).

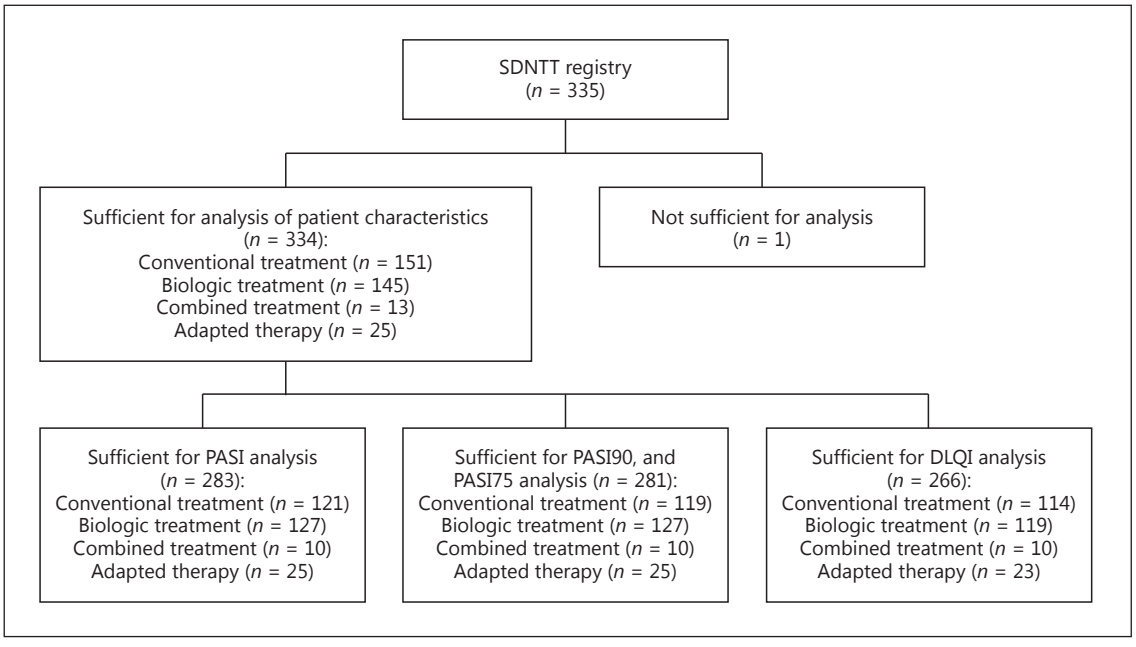

Fig. 1. Flowchart of Patients and Methods. Number of patients in the SDNTT registry included in the analysis in general and specifically in each of the outcome analyses by treatment cohort.

Results

Out of the 334 patients included in the SDNTT registry (Fig. 1), 145 received biologics (60 adalimumab, 50 ustekinumab, 31 etanercept, 4 infliximab) and 151 conventional systemic therapeutics (107 methotrexate, 22 fumaric acid esters and 19 other drugs or PUVA; Table 1). The average age was 47.1 years (SD 15) with only 39.2% women. The average body mass index (BMI) was 27.0 (SD 6.4), and the mean prior disease duration was 15 years (SD 13.5). Psoriasis arthritis was present in 23.9% over all groups.

Primary End Point PASI

Neither the biologic nor the combined treatment cohort significantly differed from the conventional systemic therapeutics cohort with regard to absolute PASI (Table 2).

Patients with therapy adaptation had on average a higher PASI than those with conventional systemic therapeutics ($p = 0.003$). At visits 3 and 4, the PASI was generally lower than at visit 2 (visit 3 vs. visit 2, $p = 0.0019$; visit 4 vs. visit 2, $p < 0.001$). The development of PASI values within 12 months was similar in all cohorts, as indicated by the non-significant interaction terms between treatment cohorts and visits. Moreover, there was a significant positive association between the PASI at baseline (visit 1) and the PASI at visits 2–4. The results from the statistical model of the log-transformed PASI are visualized on the original scale for a "model patient" in Figure 2.

Secondary End Points PASI75 and PASI90

Both the odds (and thus the probability) of a PASI90 and PASI75 were significantly increased at visits 3 and 4 compared to visit 2 (Appendix Tables). The odds of PASI75 was significantly increased with higher values of the PASI at baseline ($p < 0.001$), whereas this effect was non-significant for the PASI90. This indicates that patients with higher baseline PASI were more likely to experience a reduction of the PASI by at least 75%. Moreover, the odds of PASI90 was significantly decreased with a higher BMI ($p = 0.041$) and increased with combined therapy compared to conventional systemic therapeutics ($p = 0.043$). The results for the binary end points PASI75 and PASI90 are visualized as probabilities for a "model patient" in Figures 3 and 4.

Secondary End Point DLQI

Patients with biologic treatment reached a lower DLQI than those with conventional systemic therapeutics ($p =$

Table 1. Baseline characteristics of patients in the 4 cohorts

	Con.	Bio.	Comb.	Ada.	*p*
n	151	145	13	25	
Mean age (SD), years	46.9 (16.0)	46.6 (14.4)	50.5 (15.6)	49.6 (12.4)	0.685
Mean body size (SD), cm	170.9 (8.9)	171.4 (9.5)	174.5 (10.2)	173.5 (9.4)	0.369
Mean body weight (SD), kg	82.1 (20.5)	82.6 (21.5)	90.8 (26.1)	86.1 (21.2)	0.459
Mean body mass index (SD)	28.1 (6.5)	28.0 (6.2)	29.6 (7.6)	28.6 (6.9)	0.824
Mean years since diagnosis (SD)	15.7 (13.0)	19.7 (14.1)	20.5 (10.5)	17.5 (12.5)	0.091
Mean baseline DLQI (SD)	10.6 (6.8)	11.1 (7.6)	11.6 (9.1)	15.0 (7.0)	0.067
Mean baseline PASI (SD)	9.0 (5.9)	10.7 (7.3)	14.8 (8.9)	11.7 (7.5)	0.007
Gender female, *n* (%)	57 (37.7)	65 (44.8)	4 (30.8)	5 (20.0)	0.097
PSO arthropathy yes, *n* (%)	15 (10.2)	45 (31.0)	5 (38.5)	14 (56.0)	<0.001
Baseline medication, *n* (%)					<0.001
Adalimumab	0 (0.0)	60 (41.4)	0 (0.0)	2 (8.0)	
Combination	6 (4.1)	0 (0.0)	13 (100.0)	5 (20.0)	
Cyclosporin	5 (3.4)	0 (0.0)	0 (0.0)	2 (8.0)	
Etanercept	0 (0.0)	31 (21.4)	0 (0.0)	1 (4.0)	
Fumaric acid	22 (14.9)	0 (0.0)	0 (0.0)	3 (12.0)	
Infliximab	0 (0.0)	4 (2.8)	0 (0.0)	1 (4.0)	
Methotrexate	107 (72.3)	0 (0.0)	0 (0.0)	8 (32.0)	
Retinoid	8 (5.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Ustekinumab	0 (0.0)	50 (34.5)	0 (0.0)	3 (12.0)	

Note that due to missing values, the number of measurements is lower than the total number (top row) for some characteristics. Con., conventional; Bio., biologics; Comb., combination; Ada., adaptation; PSO, psoriasis.

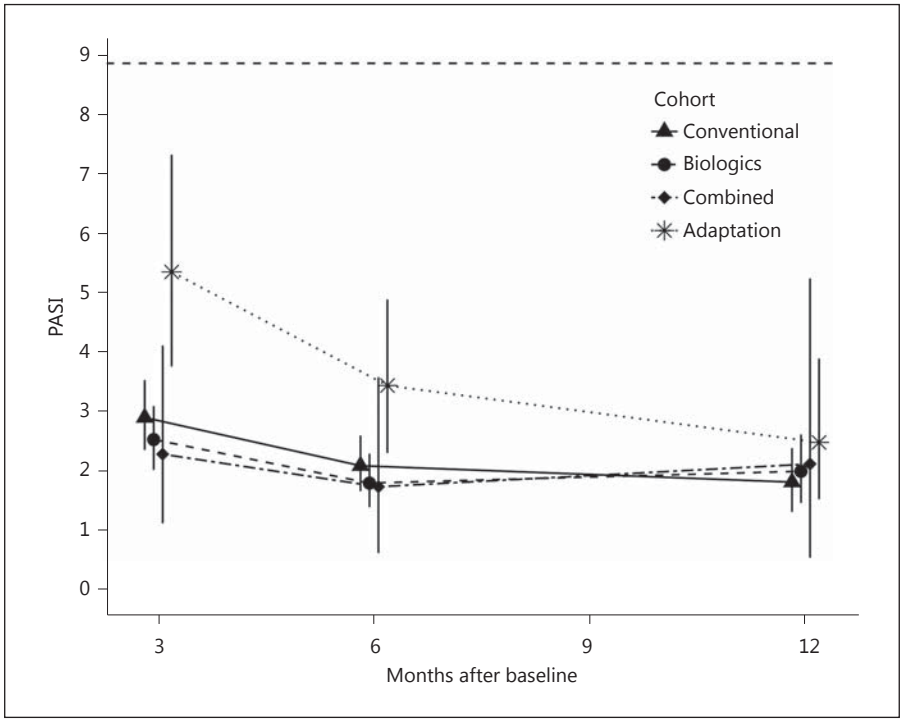

Fig. 2. Development of the PASI under different therapies. Model-based fitted values of the PASI on the original scale together with bayesian 95% credible intervals at visits 2–4 for all cohorts. The fitted values represent a male patient of median age (47.5 years), median BMI (27.0) and median baseline PASI (8.9, shown as dashed horizontal line).

Table 2. Effect size estimates with 95% confidence intervals (CI) for all predictors in the linear mixed-effects model on the log(PASI + 1)

	Estimate	95% CI	*t*	*p*
Intercept	0.490	0.219, 0.760	3.50	<0.001
log(PASI at visit 1 + 1)	0.382	0.274, 0.490	6.86	<0.001
Age	0.003	–0.002, 0.008	1.04	0.2986
Female vs. male	–0.048	–0.198, 0.102	–0.62	0.5350
BMI	0.008	–0.004, 0.019	1.30	0.1948
Biologics vs. conventional	–0.100	–0.287, 0.087	–1.04	0.2989
Combined vs. conventional	–0.173	–0.629, 0.282	–0.74	0.4622
Adaptation vs. conventional	0.490	0.178, 0.802	3.04	0.0025
Visit 3 vs. visit 2	–0.235	–0.380, –0.089	–3.13	0.0019
Visit 4 vs. visit 2	–0.329	–0.515, –0.142	–3.42	<0.001
Biologics vs. conventional at v3 vs. v2	0.000	–0.203, 0.203	0.00	0.9965
Combined vs. conventional at v3 vs. v2	0.051	–0.466, 0.566	0.19	0.8488
Adaptation vs. conventional at v3 vs. v2	–0.125	–0.458, 0.208	–0.73	0.4671
Biologics vs. conventional at v4 vs. v2	0.164	–0.093, 0.420	1.24	0.2162
Combined vs. conventional at v4 vs. v2	0.277	–0.441, 0.995	0.75	0.4547
Adaptation vs. conventional at v4 vs. v2	–0.275	–0.662, 0.112	–1.38	0.1692

v2, visit 2; v3, visit 3; v4, visit 4. The model included 283 patients.

0.001) while patients with therapy adaptation had a higher DLQI than those with conventional systemic therapeutics ($p = 0.003$). The higher the DLQI at baseline, the higher remained the DLQI during treatment ($p < 0.001$). The DLQI at visits 3 and 4 was on average lower than at visit 2 (visit 3 vs. visit 2, $p < 0.001$; visit 4 vs. visit 2, $p = 0.0026$). The results from the statistical model on the log-transformed DLQI are again visualized on the original scale for a "model patient" in Figure 5.

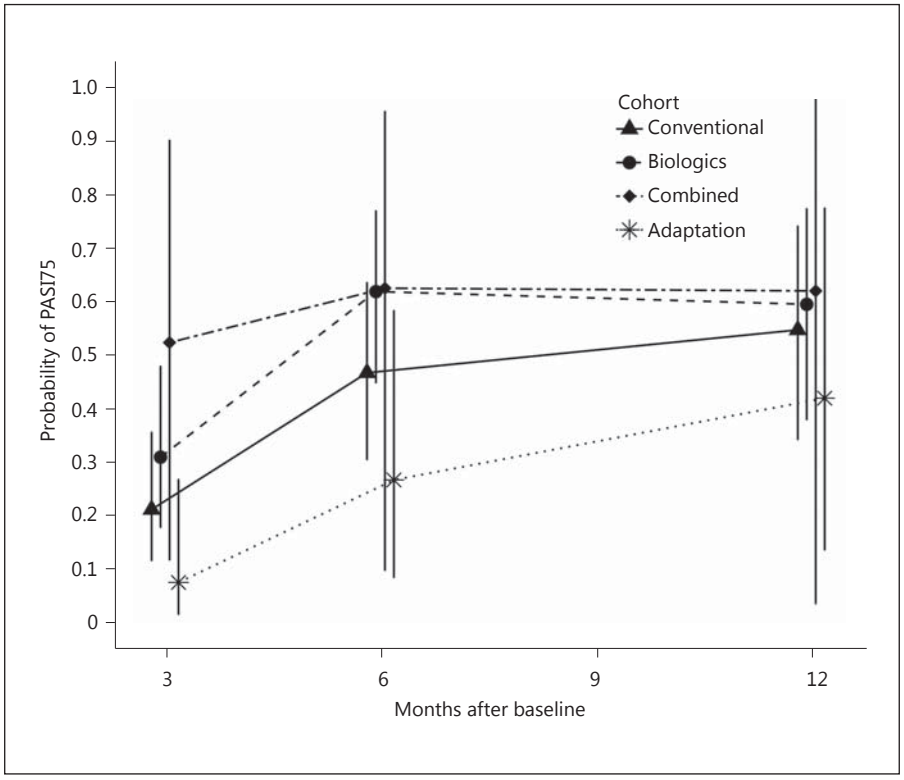

Fig. 3. Development of PASI75 under different therapies. Fitted values of the probability of PASI75 together with bayesian 95% credible intervals at visits 2–4 for all cohorts. The fitted values represent a male patient of median age (47.5 years), median BMI (27.0) and median baseline PASI (8.9).

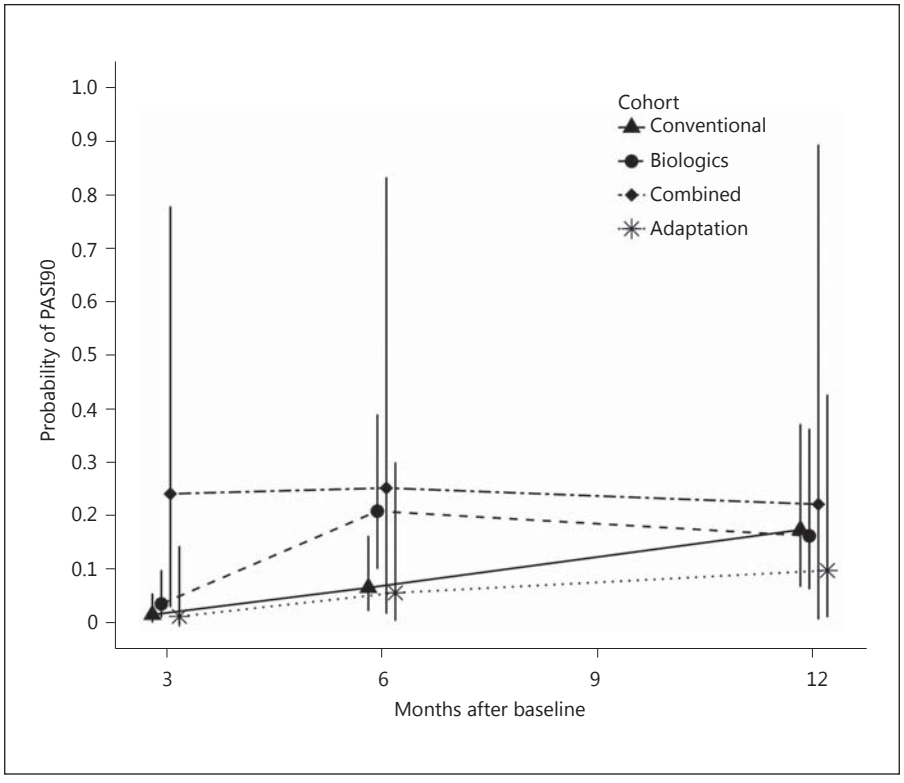

Fig. 4. Development of PASI90 under different therapies. Fitted values of the probability of PASI90 together with bayesian 95% credible intervals at visits 2–4 for all cohorts. The fitted values represent a male patient of median age (47.5 years), median BMI (27.0) and median baseline PASI (8.9).

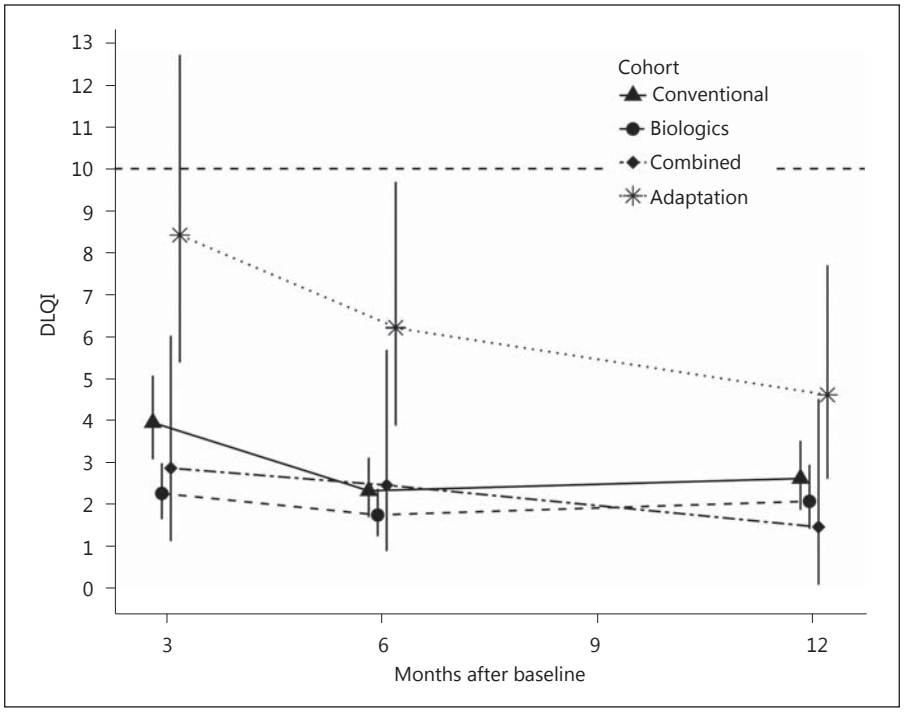

Fig. 5. Development of the DLQI under different therapies. Model-based fitted values of the DLQI on the original scale together with bayesian 95% credible intervals at visits 2–4 for all cohorts. The fitted values represent a male patient of median age (47.5 years), median BMI (27.0) and median baseline DLQI (10, shown as dashed horizontal line).

Discussion

This study investigated PASI and DLQI changes over 12 months after initiation of a systemic therapy in all psoriasis patients registered in the SDNTT registry from May 2011 to December 2014. The patient number in this study was relatively low compared to older registries of larger countries [19]; however, the results reflect the real-world situation of registered and treated patients in Switzerland. Within 12 months after the start of therapy, patients with moderate-to-severe psoriasis who were treated with biologics or combined therapy showed essentially equivalent developments of PASI values compared to those who were treated with conventional systemic therapeutics only. In comparison to those on conventional systemic therapeutics, a larger proportion of patients on biologics reached PASI75 and PASI90; however, the differences were not significant over the 12-month period. This could be due to the interrater variation by different investigators for the PASI assessment and a direct consequence that the PASI has a low resolution below values of 5 [13] (Fig. 2). As expected, patients who had to adapt treatment did not reach comparable PASI values within 12 months, as this cohort understandably represents more difficult-to-treat patients. Moreover, the limited number of patients under combined treatment had an increased probability to reach PASI90. However, real-world outcome data on combined therapy are rare, some authors concluded that combined therapy might have at least some potential benefit in patients with joint involvement, methotrexate toxicity or in cases of monotherapy failure [20].

In contrast to PASI development patients treated with biologics reached significantly lower DLQI values within 12 months compared to those treated with conventional systemic therapeutics. As in the biologic patient group psoriatic arthritis was slightly overrepresented (Table 1), the greater DLQI reduction might reflect the patient benefit of biologics on improvement of joint complaints. Presumably reduced monitoring visits, lower injection frequencies and higher drug tolerability of biologically treated patients could be feasible arguments for the better DLQI improvements. Previous studies comparing objective and subjective assessments in psoriasis patients on biologics and conventional systemic agents have been rather limited [21]. In line with our results one report also revealed more pronounced DLQI improvements in patients receiving biologics for 12 months compared to those who were on conventional systemic therapeutics [22]. We consider this finding important since the decision to initiate biologic treatment for physicians and health insurances still seems to be more strongly dependent on PASI values than on DLQI scores [23]. As stated in the recently published Swiss S1 guidelines and also based on our own results, DLQI values should be critically taken into account particularly in patients with low-

er PASI values suffering from severe involvement of difficult-to-treat locations such as the nails, scalp, genitals, palmoplantar areas or joint involvement and in those patients complaining of severe pruritus. This study has potential limitations. Due to missing values on outcomes and covariates used in the statistical models, the number of patients included in the analysis was relatively low compared to other registries [24]. However, we believe that our failure to detect significant differences regarding the primary end point PASI between either biologics or combined therapy and conventional systemic therapeutics is rather due to the small and clinically irrelevant effect sizes (e.g., PASI for biologics <0.5 points lower than for conventional systemic therapeutics after 3 months, at visit 2; Fig. 2) than due to the relatively small sample size.

The strength of this register-based study from Switzerland is that it analyses the subjective and objective disease activity under real-world conditions using robust statistical models that account for the effects of important patient characteristics, which reduce the problem of confounding. Nevertheless, some characteristics that might contribute to the outcome as well, such as details of the psoriasis location, were not captured in the SDNTT registry.

Taken together, this study shows that after 1 year of treatment, biologics are superior in improving the subjective disease burden compared to conventional systemic drugs.

Acknowledgements

The authors wish to thank all those who helped to create the SDNTT registry, all patients and all health care personnel and the SDNTT steering board.

Statement of Ethics

This research study protocol was ethically conducted in accordance with the World Medical Association Declaration of Helsinki and has been approved by the University Hospital of Basel Ethical Review Board, Switzerland. The project was conducted with informed written consent from all patients.

Disclosure Statement

The SDNTT registry has received financial support from Abbvie, Jansen and Pfizer. The sponsors had no access to data. Data collection, study design, interpretation, and analysis have been carried out with the authors' independence. All authors have participated in industry-sponsored meetings, received travel support, or served as speaker or investigator for one or more of the following companies: AbbVie, Janssen, Pfizer, Novartis, Celgene, MSD. The authors certify that they have no relevant affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, employment, stock ownership, or other equity interest, and expert testimony or patent-licensing arrangements) that would contribute to any bias in the subject matter discussed in this paper.

Appendix

Table to Figure 3

Estimates of the odds ratios (OR) with bayesian 95% credible intervals (CrI) for all predictors in the generalized linear mixed-effects model on the PASI75. The model included 281 patients. v2, visit 2; v3, visit 3; v4, visit 4.

	OR	95% CrI	*z*	*p*
Intercept	0.317	0.163, 0.630	–2.90	0.0037
PASI at visit 1 (scaled)	2.309	1.614, 3.281	3.92	<0.001
Age (scaled)	0.832	0.584, 1.162	–0.99	0.3226
Female vs. male	1.255	0.648, 2.477	0.61	0.5404
BMI (scaled)	0.927	0.665, 1.296	–0.43	0.6696
Biologics vs. conventional	1.666	0.680, 4.015	1.03	0.3044
Combined vs. conventional	4.079	0.454, 37.412	1.17	0.2427
Adaptation vs. conventional	0.309	0.060, 1.634	–1.36	0.1741
Visit 3 vs. visit 2	3.253	1.531, 6.740	2.69	0.0071
Visit 4 vs. visit 2	4.486	1.600, 11.190	2.71	0.0067
Biologics vs. conventional at v3 vs. v2	1.114	0.381, 3.168	0.19	0.8525
Combined vs. conventional at v3 vs. v2	0.467	0.026, 7.996	–0.49	0.6217
Adaptation vs. conventional at v3 vs. v2	1.347	0.222, 8.174	0.30	0.7615
Biologics vs. conventional at v4 vs. v2	0.730	0.197, 2.784	–0.44	0.6620
Combined vs. conventional at v4 vs. v2	0.331	0.006, 16.844	–0.51	0.6068
Adaptation vs. conventional at v4 vs. v2	1.936	0.241, 15.165	0.59	0.5546

Table to Figure 4

Estimates of the odds ratios (OR) with bayesian 95% credible intervals (CrI) for all predictors in the generalized linear mixed-effects model on the PASI90. The model included 281 patients. v2, visit 2; v3, visit 3; v4, visit 4.

	OR	95% CrI	z	*p*
Intercept	0.019	0.006, 0.056	–4.74	<0.001
PASI at visit 1 (scaled)	1.586	1.028, 2.489	1.89	0.059
Age (scaled)	0.783	0.505, 1.237	–1.06	0.289
Female vs. male	1.516	0.628, 3.706	0.91	0.363
BMI (scaled)	0.618	0.382, 1.013	–2.05	0.041
Biologics vs. conventional	2.126	0.561, 8.534	1.13	0.260
Combined vs. conventional	17.082	1.550, 203.568	2.02	0.043
Adaptation vs. conventional	0.819	0.065, 11.858	–0.17	0.867
Visit 3 vs. visit 2	3.914	1.280, 12.491	2.34	0.019
Visit 4 vs. visit 2	11.374	3.130, 45.604	3.34	<0.001
Biologics vs. conventional at v3 vs. v2	1.708	0.409, 7.171	0.73	0.466
Combined vs. conventional at v3 vs. v2	0.271	0.016, 4.894	–0.86	0.391
Adaptation vs. conventional at v3 vs. v2	1.041	0.060, 17.305	0.03	0.975
Biologics vs. conventional at v4 vs. v2	0.434	0.067, 2.421	–0.95	0.344
Combined vs. conventional at v4 vs. v2	0.079	0.002, 2.385	–1.26	0.208
Adaptation vs. conventional at v4 vs. v2	0.638	0.033, 12.001	–0.32	0.752

Table to Figure 5

Effect size estimates with 95% confidence intervals (CI) for all predictors in the linear mixed-effects model on the log(DLQI + 1). The model included 266 patients. v2, visit 2; v3, visit 3; v4, visit 4.

	Estimate	95% CI	*t*	*p*
Intercept	0.588	0.259, 0.918	3.45	<0.001
log(DLQI at visit 1 + 1)	0.425	0.301, 0.549	6.65	<0.001
Age	0.001	–0.006, 0.008	0.16	0.8735
Female vs. male	–0.034	–0.239, 0.171	–0.32	0.7466
BMI	0.006	–0.009, 0.022	0.79	0.4312
Biologics vs. conventional	–0.417	–0.661, –0.173	–3.31	0.0010
Combined vs. conventional	–0.248	–0.838, 0.343	–0.81	0.4176
Adaptation vs. conventional	0.642	0.223, 1.060	2.97	0.0032
Visit 3 vs. visit 2	–0.398	–0.570, –0.225	–4.49	<0.001
Visit 4 vs. visit 2	–0.314	–0.514, –0.113	–3.04	0.0026
Biologics vs. conventional at v3 vs. v2	0.227	–0.014, 0.469	1.82	0.0689
Combined vs. conventional at v3 vs. v2	0.287	–0.298, 0.872	0.95	0.3411
Adaptation vs. conventional at v3 vs. v2	0.132	–0.257, 0.520	0.66	0.5112
Biologics vs. conventional at v4 vs. v2	0.255	–0.030, 0.541	1.73	0.0839
Combined vs. conventional at v4 vs. v2	–0.137	–0.894, 0.625	–0.35	0.7270
Adaptation vs. conventional at v4 vs. v2	–0.203	–0.642, 0.237	–0.90	0.3714

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